PATENT COOPERATION TREATY

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From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

Stones, James Alexander
Beck Greener
Fulwood House
12 Fulwood Place
London WC1V 6HR
GRANDE BRETAGNE

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(PCT Rule 71.1)

Date of mailing *(day/month/year)*	02.06.2006

Applicant's or agent's file reference	IMPORTANT NOTIFICATION
AFB/JAS/P10272WO	

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB2005/000415	07.02.2005	13.02.2004

Applicant
TILLOTTS PHARMA AG

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary report on patentability and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority:	Authorized Officer
European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Rossi, C Tel. +31 70 340-3322

Form PCT/IPEA/416 (January 2004)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference AFB/JAS/P10272WO	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/GB2005/000415	International filing date *(day/month/year)* 07.02.2005	Priority date *(day/month/year)* 13.02.2004
International Patent Classification (IPC) or national classification and IPC INV. A61K9/48		
Applicant TILLOTTS PHARMA AG		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 4 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in celectronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☒	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
26.01.2006	02.06.2006

Name and mailing address of the international preliminary examining authority:	Authorized officer
European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Gomez Gallardo, S Telephone No. +31 70 340-9546

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/GB2005/000415

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-11 as originally filed

   Claims, Numbers

   1-29 received on 26.01.2006 with letter of 20.01.2006

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 25,26, with regard to industrial applicability

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 25,26, with regard to industrial applicability

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-29
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-29
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-24,27-29
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (SEPARATE SHEET)

International application No. PCT/GB2005/000415

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

For the assessment of the present claims 25 and 26 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such compound for the manufacture of a medicament for a new medical treatment.

Re Item V

Reasoned statement with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement

1. CITED DOCUMENTS

Reference is made to the following document:

D1: EP-A-0 289 204 (EFAMOL HOLDINGS PLC) 2 November 1988 (1988-11-02) (cited in the application)

2. CLARITY (Art. 6 PCT and Rule 6.2(a) PCT)

Claims 27-29 contravene the requirements of Article 6 PCT in combination with Rule 6.2(a) PCT since they rely, in respect of the technical features of the invention, on references to the description ("*with reference to the accompanying examples*").

3. NOVELTY (Art. 33(2) PCT) AND INVENTIVE STEP (Art. 33(3) PCT)

The document D1 is regarded as being the closest prior art to the subject-matter of the

present application and discloses (cf. page 8 - page 9, examples 1, 2 and 4) soft gelatin capsules comprising lithium eicosapentaenoate (omega-3 polyunsaturated fatty acid formulation). According to the description of the present application (cf. page 2, paragraph 2), *"the vast majority of soft gelatin capsules are manufactured from Type B gelatin"*. Therefore, it is assumed that the gelatin disclosed in D1 is of Type B.

The subject-matter of the present application differs from D1 (a) in that the omega-3 polyunsaturated fatty acid formulation is in free acid form and (b) in that the capsule comprises gelatin extracted by an extraction process comprising acid pre-treatment of a collagen source (gelatin Type A). Therefore, the subject-matter of present claims 1-29 is new in the sense of Articles 33(1) and (2) PCT.

The effect of the capsule having gelatin extracted by an extraction process comprising acid pre-treatment of a collagen source (gelatin Type A) is a significantly lower rate of hardening, which translates into an increased shelf life for the capsule. The objective technical problem to be solved by the present application may therefore be regarded as the provision of an improved soft gelatin capsule, comprising at least one omega-3 polyunsaturated fatty acid formulation, that displays a reduced hardening rate and thereby has an increased shelf life. The solution proposed in the present application is not suggested in D1. There is no other document in the prior art that would have prompted the skilled person, faced with the objective technical problem, to modify or adapt the teaching of D1 in order to arrive at the claimed solution. As an additional aspect, the use of gelatin Type A (made from pig skin) avoids any risk of transmission of spongiform encephalopathies from gelatin made from bovine bones and hides. In view of this, claims 1-29 involve an inventive step in the sense of Article 33(3) PCT.

4. INDUSTRIAL APPLICABILITY (Rule 67.1(iv) PCT, Art. 34(4)(a)(i) PCT and Art. 33(4) PCT)

Claims 25 and 26 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Claims 1-24 and 27-29 satisfy the criterion of industrial applicability set forth in Article 33(4) PCT.

Re Item VI

Certain documents cited

Certain published documents

Application No Patent No	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date *(valid claim)* *(day/month/year)*
WO2004/091317	28/10/2004	14/04/2004	17/04/2003

CLAIMS

1. A soft gelatin capsule containing a pharmaceutical formulation comprising at least one omega-3 polyunsaturated fatty acid in free acid form characterised in that the capsule comprises gelatin extracted by an extraction process comprising acid pre-treatment of a collagen source.

2. A soft gelatin capsule as claimed in Claim 1 wherein formulation comprises 5, 8, 11, 14, 17-eicosapentaenoic acid (or "EPA").

3. A soft gelatin capsule as claimed in Claim 2 wherein EPA is present in an amount of at least about 50 wt % of the formulation.

4. A soft gelatin capsule as claimed in Claim 2 or Claim 3 wherein EPA is present in an amount of between from about 50 wt % to about 60 wt % of the formulation.

5. A soft gelatin capsule as claimed in Claim 2 or Claim 3 wherein EPA is present in an amount of at least about 90 wt % of the formulation.

6. A soft gelatin capsule as claimed in any of the preceding claims wherein the formulation comprises 4, 7, 10, 13, 16, 19-docosahexaenoic acid (or "DHA").

7. A soft gelatin capsule as claimed in Claim 6 insofar as dependent from any of Claims 1 to 4 wherein DHA is present in an amount of between from about 20 wt % to about 30 wt % of the formulation.

8. A soft gelatin capsule as claimed in any of the preceding claims comprising between from about 100mg to about 2000mg of said formulation.

9. A soft gelatin capsule as claimed in any of the preceding claims comprising about 500mg of said formulation.

10. A soft gelatin capsule as claimed in any of Claims 1 to 8 comprising about 1000mg of said formulation.

11. A soft gelatin capsule as claimed in any of the preceding claims wherein the gelatin comprises porcine gelatin.

12. A soft gelatin capsule as claimed in any of Claims 1 to 10 wherein the gelatin comprises bovine gelatin.

13. A soft gelatin capsule as claimed in any of Claims 1 to 10 wherein the gelatin comprises fish gelatin.

14. A soft gelatin capsule as claimed in any of the preceding claims wherein the wall of the capsule consists of a single layer.

15. A soft gelatin capsule as claimed in any of the preceding claims wherein the capsule delays release of the formulation until after passage through the stomach.

16. A soft gelatin capsule as claimed in any of the preceding claims wherein the capsule delays release of the formulation until after passage beyond the pancreatic duct in the duodenum.

17. A soft gelatin capsule as claimed in Claim 15 or Claim 16 wherein the capsule is coated with at least one enteric material.

18. A soft gelatin capsule as claimed in any of Claims 15 to 17 wherein at least one enteric material is integrated within the gelatin of the capsule.

19. A soft gelatin capsule as claimed in Claim 17 or Claim 18 wherein the or at least one enteric material is a neutral polyacrylate polymer.

20. A soft gelatin capsule as claimed in any of Claims 17 to 19 wherein the or at least one enteric material is poly(ethylacrylate-methylmethacrylate).

21. Use of at least one omega-3 polyunsaturated fatty acid in free acid form in the manufacture of a medicament comprising at least one soft gelatin capsule containing a pharmaceutical formulation comprising at least one omega-3 polyunsaturated fatty acid in free acid form characterised in that the capsule comprises gelatin extracted by an extraction process comprising acid pre-treatment of a collagen source for the oral treatment or prophylaxis of a condition selected from chronic inflammatory conditions, hyperlipidaemia, hypertriglyceridaemia, asthma, bipolar disorder and neoplastic disease.

22. Use as claimed in Claim 21 wherein the medicament comprises at least one soft gelatin capsule as defined in any of Claims 2 to 20.

23. A process for the manufacture of a soft gelatin capsule containing a pharmaceutical formulation comprising at least one omega-3 polyunsaturated fatty acid in free acid form, said process comprising encapsulating said pharmaceutical formulation in gelatin extracted by an extraction process comprising acid pre-treatment of a collagen source.

24. Use of gelatin extracted by an extraction process comprising acid pre-treatment of a collagen source in a soft gelatin capsule containing a pharmaceutical formulation comprising at least one omega-3 polyunsaturated fatty acid in free acid form to improve shelf life of the soft gelatin capsule, wherein said shelf life is greater than that for a soft gelatin capsule containing a pharmaceutical formulation comprising at least one omega-3 polyunsaturated fatty acid in free acid form in which the gelatin consists essentially of gelatin extracted by an extraction process comprising alkali pre-treatment of a bovine collagen source.

25. A method of treatment or prophylaxis of a condition selected from chronic inflammatory conditions, hyperlipidaemia, hypertriglyceridaemia, asthma, bipolar disorder and neoplastic disease comprising administering a therapeutically effective amount of a pharmaceutical formulation comprising at least one omega-3 polyunsaturated fatty acid in free acid form per day in the form of a plurality of soft gelatin capsules containing a pharmaceutical formulation comprising at least one omega-3 polyunsaturated fatty acid in free acid form characterised in that the capsule

comprises gelatin extracted by an extraction process comprising acid pre-treatment of a collagen source.

26. A method as claimed in Claim 25 wherein the soft gelatin capsules are as defined in any of Claims 2 to 20.

27. A soft gelatin capsule substantially as hereinbefore described with reference to the accompanying examples.

28. A process substantially as hereinbefore described with reference to the accompanying examples.

29. A use substantially as hereinbefore described with reference to the accompanying examples.